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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/521,410	01/18/2005	Axel Ullrich	2923-679	7025

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ROTHWELL, FIGG, ERNST & MANBECK, P.C.
1425 K STREET, N.W.
SUITE 800
WASHINGTON, DC 20005

EXAMINER	
REDDIG, PETER J	

ART UNIT	PAPER NUMBER
1642	

NOTIFICATION DATE	DELIVERY MODE
06/01/2007	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

PTO-PAT-Email@rfem.com

Office Action Summary	Application No.	Applicant(s)	
	10/521,410	ULLRICH ET AL.	
	Examiner	Art Unit	
	Peter J. Reddig	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 January 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-34* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-34* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Restriction is required under 35 U.S.C. 121 and 372.

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1.

In accordance with 37 CFR 1.499, applicant is required, in reply to this action, to elect a single invention to which the claims must be restricted.

Group 1, claim(s) 1-9, drawn to a method of determining the invasivity of malignant disorders comprising measuring the expression of at least one gene selected from the group consisting of AXL, GAS, MMP14, ADAM12, ADAM17, MT3MMP, FGF2, FGF5, FYN, LYN, DDR2, TIMP1, HBEGF, SGF, S6KII, MAP4K4, SIRPα, Annexin 2, Stat 5b and EDG2 wherein a high expression correlates with a high invasivity.

It is noted that the number of combinations of genes to be measured claimed, as calculated by factorial analysis, is $2.4x10^{18}$, that is $20! = 2.4x10^{18}$. Thus, the claims are drawn to $2.4x10^{18}$ distinct inventions. Applicant is required to identify and elect one gene or a specific, defined single combination of genes for examination. It is further noted, for Applicant's convenience, that this is not a requirement for the election of species, but rather a requirement for the election of a single distinct invention for examination. The claims will be examined as drawn to the elected invention.

Group 2, claim(s) 10-21, drawn to a method of reducing the invasivity of malignant disorders comprising inhibiting the AXL gene expression and/or AXL ligand gene expression and/or protein function and/or protein ligand function.

It is noted that the number of combinations of AXL or AXL ligand genes and proteins to be inhibited claimed, as calculated by factorial analysis, is 24, that is $4! = 24$. Thus, the claims are drawn to 24 distinct inventions. Applicant is required to identify and elect one AXL or AXL ligand gene or protein or a specific, defined single combination of AXL or AXL ligand genes oe proteins to be inhibited for examination. It is further noted, for Applicant's convenience, that this is not a requirement for the election of species, but rather a requirement for the election of a single distinct invention for examination. The claims will be examined as drawn to the elected invention, i.e. for claim 15 an inhibitor of the Axl gene would only be examined if Axl gene expression was elected alone or in combination.

Group 3, claim(s) 22-30, drawn to a pharmaceutical composition comprising as an active agent an inhibitor of the AXL gene, AXL ligand gene, AXL protein and/or AXL protein ligand together with pharmacologically active diluents, carriers and/or adjuvants.

It is noted that the number of combinations of AXL or AXL ligand genes and proteins, as calculated by factorial analysis, is 24, that is 4! =24. Thus, the claims are drawn to 24 distinct inventions. Applicant is required to identify and elect one AXL or AXL ligand gene or protein or a specific, defined single combination of AXL or AXL ligand genes or proteins for examination. It is further noted, for Applicant's convenience, that this is not a requirement for the election of species, but rather a requirement for the election of a single distinct invention for examination. The claims will be examined as drawn to the elected invention.

Group 4, claim(s) 31-34, drawn to a method of identifying and/or characterizing an inhibitor of the invasivity of malignant disorders comprising determining, if a test compound is capable of inhibiting the AXL gene, AXL ligand gene, AXL protein and/or AXL protein ligand.

It is noted that the number of combinations of AXL or AXL ligand genes and proteins to be inhibited, as calculated by factorial analysis, is 24, that is 4! =24. Thus, the claims are drawn to 24 distinct inventions. Applicant is required to identify and elect one AXL or AXL ligand gene or protein or a specific, defined single combination of AXL or AXL ligand genes or proteins to be inhibited for examination. It is further noted, for Applicant's convenience, that this is not a requirement for the election of species, but rather a requirement for the election of a single distinct invention for examination. The claims will be examined as drawn to the elected invention.

The technical feature linking Groups 1-4 appears to be AXL gene expression. A national stage application shall relate to one invention only or to a group of inventions so linked as to form a single general inventive concept. Unity of invention is fulfilled only when there is a technical relationship among the inventions involving one or more of the same or corresponding special technical features which define a contribution over the prior art. If there is no special technical feature, if multiple products, processes of manufacture or uses are claimed, the first invention of the category first mentioned in the claims of the application will be considered as the main invention in the claims, see PCT article 17(3) (a) and 1.476 (c), 37 C.F.R. 1.475(d).

The inventions listed as Groups 1-4 do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

The technical feature linking Groups 1-4 appears to be AXL gene expression.

However, Meric *et al.* (Clinical Cancer Research, Vol. 8, pages 361-371, February 2002) teach measuring AXL gene expression in breast cancer cell lines, see Abstract and Figure 4. Additionally, Meric et al. teach that the Axl gene is overexpressed in thyroid and hepatocellular cancer and metastatic prostate and colon cancers, see p. 366, left col.

Therefore, the technical feature linking the inventions of Groups 1-4 does not constitute a special technical feature as defined by PCT Rule 13.2 as it does not define a contribution over the prior art.

Species Elections for Group 1

A. Claim 1 is generic to the following disclosed patentably distinct species of the form of expression determination:

1) on the mRNA level

2) on the protein level

Species Elections for Group 2

A. Claim 10 is generic to the following disclosed patentably distinct species of the form of inhibitor:

1) an antisense nucleic acid directed against the Axl gene or a transcript

2) a ribozyme directed against the Axl gene or a transcript

3) a RNA interference molecule directed against the Axl gene or a transcript

4) a dominant-negative mutant of the Axl gene

5) an antibody directed against the Axl protein

The elected species should be commensurate in scope with the AXL genes or proteins or AXL ligand genes or proteins combinations elected for Group 2 above.

Species Elections for Group 3

A. Claim 22 is generic to the following disclosed patentably distinct species of the form of inhibitor:

1) an antisense nucleic acid directed against the Axl gene or a transcript

2) a ribozyme directed against the Axl gene or a transcript

3) a RNA interference molecule directed against the Axl gene or a transcript

4) a dominant-negative mutant of the Axl gene

5) an antibody directed against the Axl protein

The elected species should be commensurate in scope with the AXL genes or proteins or AXL ligand genes or proteins combinations elected for Group 2 above.

The above species are independent or distinct because they comprise structurally distinct molecules and have different modes of operation and different effects. Further, each species would require different searches and the consideration of different patentability issues.

Applicant is required under 35 U.S.C. 121 to elect a single disclosed species from each species group above for the elected invention Group, even though this requirement is traversed. Applicant is advised that a reply to this requirement must include an identification of the species that is elected consonant with this requirement, and a listing of all claims readable thereon, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election.

Should applicant traverse on the ground that the species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the

examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103 of the other invention.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which depend from or otherwise require all the limitations of an allowable generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and the product claims are subsequently found allowable, withdrawn process claims that depend from or otherwise require all the limitations of the allowable product claim will be considered for rejoinder. All claims directed to a nonelected process invention must require all the limitations of an allowable product claim for that process invention to be rejoined.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103 and 112. Until all claims to the elected product are found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowable product claim will not be rejoined. See MPEP § 821.04(b). Additionally, in order to retain the right to rejoinder in accordance with the above policy, applicant is advised that the process claims should be amended during prosecution to require the limitations of the product claims. **Failure to do so**

may result in a loss of the right to rejoinder. Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Applicant is advised that the reply to this restriction requirement to be complete must include an election of the invention to be examined even though the requirement is traversed (37 CFR 1.143).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Peter J. Reddig whose telephone number is (571) 272-9031. The examiner can normally be reached on M-F 8:30 a.m.-5:00 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shanon Foley can be reached on (571) 272-0898. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

SUSAN UNGAR, PH.D
PRIMARY EXAMINER

Peter J. Reddig, Ph.D.
Examiner
Art Unit 1642

PJR